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THE REPORT OF PRESIDENT TRUMAN ON THE ATOMIC BOMB

SIXTEEN hours ago an American airplane dropped one bomb on Hiroshima, an important Japanese army base. That bomb had more power than 20,000 tons of TNT. It had more than 2,000 times the blast power of the British "Grand Slam," which is the largest bomb ever yet used in the history of warfare.

The Japanese began the war from the air at Pearl Harbor. They have been repaid manyfold. And the end is not yet. With this bomb we have now added a new and revolutionary increase in destruction to supplement the growing power of our armed forces. In their present form these bombs are now in production and even more powerful forms are in development.

It is an atomic bomb. It is a harnessing of the basic power of the universe. The force from which the sun draws its power has been loosed against those who brought war to the Far East.

Before 1939, it was the accepted belief of scientists that it was theoretically possible to release atomic energy. But no one knew any practical method of doing it.

By 1942, however, we knew that the Germans were working feverishly to find a way to add atomic energy to the other engines of war with which they hoped to enslave the world. But they failed. We may be grateful to Providence that the Germans got the V1's and the V2's late and in limited quantities and even more grateful that they did not get the atomic bomb at all.

The battle of the laboratories held fateful risks for us as well as the battles of the air, land and sea, and we have now won the battle of the laboratories as we have won the other battles.

Beginning in 1940, before Pearl Harbor, scientific knowledge useful in war was pooled between the United States and Great Britain, and many priceless helps to our victories have come from that arrangement. Under the general policy the research on the atomic bomb was begun. With American and British scientists working together we entered the race of discovery against the Germans.

The United States had available the large number of scientists of distinction in the many needed areas of knowledge. It had the tremendous industrial and financial resources necessary for the project and they could be devoted to it without undue impairment of other vital war work.

In the United States the laboratory work and the production plants, on which a substantial start had already been made, would be out of reach of enemy bombing, while at that time Britain was exposed to constant air attack and was still threatened with the possibility of invasion.

For these reasons Prime Minister Churchill and President Roosevelt agreed that it was wise to carry on the project here. We now have two great plants and many lesser works devoted to the production of atomic power. Employment during peak construction numbered 125,000 and over 65,000 individuals are even now engaged in operating the plants. Many have worked there for 2½ years. Few know what they have been producing. They see great quantities of material going in and they see nothing coming out of these plants, for the physical size of the explosive charge is exceedingly small.

We have spent $2,000,000,000 on the greatest scientific gamble in history and won.

But the greatest marvel is not the size of the enterprise, its secrecy or its cost, but the achievement of scientific brains in putting together infinitely complex pieces of knowledge held by many men in different fields of science into a workable plan. And hardly less marvelous has been the capacity of industry to design, and of labor to operate, the machines and methods to do things never done before so that the brain child of many minds came forth in physical shape and performed as it was supposed to do.

Both science and industry worked under the direction of the United States Army, which achieved a unique success in managing so diverse a problem in the advancement of knowledge in an amazingly short time.

It is doubtful if such another combination could be got together in the world. What has been done is the greatest achievement of organized science in history. It was done under high pressure and without failure.

We are now prepared to obliterate more rapidly and completely every productive enterprise the Japanese have above ground in any city. We shall destroy their docks, their factories and their communications. Let there be no mistake; we shall completely destroy Japan's power to make war.

It was to spare the Japanese people from utter destruction that the ultimatum of July 26 was issued at Potsdam. Their leaders promptly rejected that ultimatum. If they do not now accept our terms they may expect a rain of ruin from the air, the like of which has never been seen on this earth. Behind this air attack will follow sea and land forces in such numbers and power as they have not yet seen and with the fighting skill of which they are already well aware.

The Secretary of War, who has kept in personal touch with all phases of the project, will immediately make public a statement giving further details.

His statement will give facts concerning the sites at Oak Ridge near Knoxville, Tenn., and at Richmond near Pasco, Wash., and an installation near Santa Fe, N. Mex. Although the workers at the sites have been making materials to be used in producing the greatest destructive force in history, they have not themselves been in danger beyond that of many other occupations, for the utmost care has been taken of their safety.

The fact that we can release atomic energy ushers in a new era in man's understanding of nature's forces. Atomic energy may in the future supplement the power that now comes from coal, oil and falling water, but at present it can not be produced on a basis to compete with them commercially. Before that comes there must be a long period of intensive research.

It has never been the habit of the scientists of this country or the policy of this Government to withhold from the world scientific knowledge. Normally, therefore, everything about the work with atomic energy would be made public.

But under present circumstances it is not intended to divulge the technical processes of production or all the military applications, pending further examina-

tion of possible methods of protecting us and the rest of the world from the danger of sudden destruction.

I shall recommend that the Congress of the United States consider promptly the establishment of an appropriate commission to control the production and use of atomic power within the United States. I shall give further consideration and make further recommendations to the Congress as to how atomic power can become a powerful and forceful influence towards the maintenance of world peace.

MICROSCOPIC AND CHEMICAL PROPERTIES OF PRECANCEROUS LESIONS[1,2]

By Dr. E. V. COWDRY

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WHEN cells become cancerous they undergo a transformation, said to be malignant, because thereafter they and their descendants behave like criminals unrestrained by the controls which shape the behavior of their normal neighbors. We know that a great many agents, called carcinogens, can produce this change and further that there is a long interval, usually amounting to several years, between their initial action and the final transformation. A carcinogen may act once, or repeatedly, or be succeeded by another carcinogen, and modifying conditions often operate tending to facilitate or to inhibit the production of cancer. Long before the actual expression of malignant behavior by the cells it is often possible to demonstrate that these have been changed and are, therefore, far from normal.

The designation "precancerous lesion" is applied to a type of structural change in a tissue in which clinical experience shows that the cells are more likely to become malignant than in other kinds of lesions. Several types have been recognized: in the skin, pigmented moles of the junction type and senile keratotic areas; in the breast and uterus, chronic inflammatory lesions; in the colon, polypoid adenomas; and so on. But, when the fate of many individual lesions belonging to a single type is followed, it usually happens that the malignant transformation only takes place in but a few of them. The majority of the individual lesions are not in fact precancerous. The adjective "precancerous" relates to the type, not to the particular lesion. Perhaps two sorts of lesions are grouped under a single type, or they are all of one kind and some happen to be exposed to a carcinogen not acting on the majority.

Even with such outspoken lesions, some of which become malignant, it is not possible to localize the actual transformation to cells which are multiplying more rapidly or more slowly than normal; because, in a given lesion whether hypertrophic or atrophic, a few cells may not be acting like the majority which give character to it.

The problem is further complicated by our inability to discover any type of cell in the body capable of multiplication, or which can become so, which never undergoes a malignant transformation. We have to face the possibility that for each and every one of them a precancerous condition may occasionally develop which is individual and distinctive and depends on structural modifications which may or may not be demonstrable microscopically. When clinicians are confronted with lesions of a precancerous type they seldom know what caused them and they can not evaluate all the possibly modifying factors which have participated through the years in their development and persistence. It is high time that the problem be brought into the laboratory, where the precancerous type of lesion can be produced at will by a standardized technique in experimental animals and its evolution can be followed in a few weeks time. Indeed the main research project in the Barnard Hospital is analysis of the biological equation:

Chemically pure carcinogen (methylcholanthrene) + epidermis (an avascular tissue composed of cells of a single type) of closely inbred strain of mice = squamous cell carcinoma in a very high percentage of animals.

This analysis is limited to the properties of epidermis that can be quantitatively determined. Our purpose is integrative, to discover whether the properties increase, decrease or remain constant; and, when there is a change in a property, whether it is paralleled by alterations in other properties. It is, of course, not feasible to investigate many properties in one and the same group of mice. Nevertheless, by standardizing the equation through elimination of the principal variables, the observations made on properties in different lots of mice can in a sense be superimposed.

[1] From the Department of Anatomy, Washington University School of Medicine, St. Louis, Missouri, and The Barnard Free Skin and Cancer Hospital.

[2] Adam M. Muller Memorial Lecture, Long Island College of Medicine, April 23, 1945.

Because each property studied is to some extent a problem in itself, though an integral part of the whole, the papers by various members of the team are units. This is helpful, for it promotes individual initiative, gives credit where it is due and makes it unnecessary to head the contributions by a long series of names of authors.

In the past seven years the following investigators have published papers advancing this project: V. M. Albers, J. P. Baumberger, J. J. and M. McA. Biesele, Z. K. Cooper, E. V. Cowdry, Wm. Cramer, H. I. Firminger, H. C. Franklin, C. E. Lischer, P. F. Max, B. Milder, F. X. Paletta, H. C. Reller, A. Schiff, W. L. Simpson, R. E. Stowell, V. Suntzeff, H. C. Thompson, F. Urban, L. F. Wicks and D. Ziegler. Their contributions are specified in a recent report.[3] They have worked in the laboratories of Barnard Hospital or of Washington University, or to a less extent in those of the C. F. Kettering Foundation for the Study of Chlorophyll and Photosynthesis at Antioch College. Without financial aid, gratefully acknowledged in the same report, but little progress could have been made.

By fluorescence microscopy and spectrography the carcinogen has been followed into the skin, where it soon disappears as such. Other fluorescent compounds make their apparance. To unravel them is quite a task. But a glimpse has been obtained of the conditions, somehow established in the epidermis by the carcinogen, which antedate the expression of malignant behavior by the altered cells. These include a new chemical equilibrium the discovery of which was made possible by devising a method for the removal of epidermis from dermis in a state suitable for chemical analysis and by adapting polarographic and other techniques to epidermis. As has been reported in various papers this equilibrium is characterized by marked decreases from the normal in calcium, iron and lipid; while sodium, potassium, magnesium and ascorbic acid show no noteworthy changes. In addition, unpublished observations by Wicks and Suntzeff reveal a decrease in cholesterol; of Carruthers and Suntzeff, a decrease in copper and zinc; and of Tatum, Ritchey and Cowdry, a decrease in biotin. The new equilibrium is established promptly, within less than 10 days, and is maintained, with but slight variations equally balanced, for several weeks (a long time in the life of mice) until the malignant transformation makes its appearance in a few cells.

Obviously we must learn more about this new equilibrium. Other properties may be found to remain constant during this period and still others, in this relatively steady chemical environment, to change slowly or suddenly. The equilibrium, whatever its limitations, is created by the reacting cells and they in turn are subject to it. The new lives which they and their descendants live during this long period, on amounts of iron, calcium, cholesterol, copper and biotin reduced approximately 50 per cent., are likely to be very different from the normal. We find that the cells are larger, and that the increase in volume is greater in the cytoplasm than in the nucleus so that the nucleocytoplasmic ratio is decreased and remains at about the same level (when graphically expressed) during the whole period. As early as 12 hours after a single application of carcinogen there is a striking increase in the cytoplasmic content of ribonucleic acid, which attains a maximum from the 3rd to the 10th day, and then decreases. The rate of mitosis increases progressively, attains a high level, which is sustained for days, only to fall and rise again just before the time when cancers show themselves. An enlargement, usually a doubling of chromosomes (measured in the metaphase), noticeable on the second day, is manifested by 13 per cent. of metaphases on the third day, after which it is apparently maintained at a somewhat lower frequency to the fifty-seventh day. Thymonucleic acid is increased and the displaceability of basophilic chromatin and nucleoli, when subjected to ultracentrifugal force, is increased. This suggests a fundamental decrease in intranuclear viscosity. Thus, what little evidence we have is consistent with the prevalent idea that the malignant transformation is conditioned by some change in the nucleus. A technique, recently devised for separating out the nuclei from epidermis, and their collection *en masse*, opens up several attractive lines of investigation.

But *where* and *when* the transformation occurs elude us. Concerning the first, several observations point to the spinous layer. We do not know why the change is restricted to one or more small foci, nor why most of the epidermis treated with the carcinogen does not react to it by cancer production. But, if the malignant transformation is conditioned by a mutation, it would hardly be expected to appear in a very large proportion of the cellular population. Generally speaking, a mutation occurs in but a few of a great many cells or organisms, all of which have been subjected to the influence bringing it about.

Our analyses are of treated epidermises from several mice taken together to give sufficient amounts. Therefore we have no means of knowing how uniformly the new conditions prevail in our specimens. Yet we think that the malignant change originates in an area or areas in which the new equilibrium, or a condition closely resembling it, has previously been established.

[3] *Jour. Invest. Dermat.*, 6: 15–42, 1945.

Evidence for this assumption is found in a less complete study of the conditions of cell life in a resulting transplantable carcinoma. To analyze any and all tumors developing from transplants of this carcinoma in mice is as futile as to analyze skin consisting of epidermis plus dermis. Experience has shown that to obtain worthwhile data the analyses must be limited to very small young tumors in which necrotic material is not a complicating factor. The chemical composition of such tumors—almost devoid of dead material, and therefore largely made up of active cancer cells—is, as far as we know it, in an equilibrium which definitely seems to be a carry-over from the pre-existing new equilibrium of the hyperplastic epidermis. Thus, the decrease in iron, noted in the hyperplastic epidermis, is found also in the cancer; while the decreases in calcium and copper and the increase in displaceability of nuclear contents, characteristic of the hyperplastic epidermis, are all carried to a greater degree in cancer.

Accurately to state *when,* after the first treatment with carcinogen, the malignant transformation takes place is beyond us. The new equilibrium is established long before any epidermal cells break loose and behave in a malignant fashion. However, the possibility must be borne in mind that a few cells may undergo this fundamental change early in the reaction and are unable to behave malignantly because they are, at least for a time, so closely bound together in a tissue remarkable for the tightness of cellular connections. Perhaps some hitherto unrecognized spreading factor later operates to break down the cellular connections and also to liquefy the ground substance of the dermis in this fashion facilitating detachment and invasion. This idea stems from the curious behavior of the mast cells in the dermis.

In our experimental material we set the stage by arranging for the same carcinogen to act to the same degree on the same tissue of mice of the same closely inbred strain for selected lengths of time. In so-called precancerous lesions in man we can only take what we can get unarmed by such accurate information, yet definite progress is feasible in several directions. Precancerous lesions of the skin and of the mucous membrane of the mouth and vulva are the most susceptible of attack because they are easily seen and samples can readily be collected as biopsy specimens. Not all carcinogens are fluorescent, but it would be a simple matter quickly to search for fluorescent ones by the techniques used. Since the epithelial components can be separated from the underlying tissue by the heat method, they can be collected in suitable condition for chemical analysis. Because these lesions persist for long years without grossly noticeable change—in fact for periods occupying roughly the same fraction of the human life span as the new equilibrium does that of mice—it is probable that these human cells are also, at least in some respects, in a new equilibrium, or balanced state, differing from that of corresponding normal tissue. It would be interesting to determine whether this equilibrium is the same in individual lesions of the same clinical type and, by so doing, to check the possibility already mentioned that the lesions, though looking alike, may be of different sorts, and that this difference may explain the fact that the malignant transformation only appears in some of them. It would also be worthwhile to compare the new equilibria, if such are present, in atrophic and hypertrophic lesions with each other and with the one which we have noted in our series. These and many other opportunities present themselves, including efforts to heal the lesions by reconstituting the old normal equilibrium.

In conclusion, I wish to explain that these measurements of the properties of epidermis subjected to methylcholanthrene before malignancy sets in, are but part of the principal Barnard Hospital cancer project. They may be considered as work on the first and lowest level in this project, for we are building constructively. Obviously such studies are limited merely by the number of properties that can be investigated quantitatively, and the more included the more valuable their integration becomes.

Work on the second level is restricted to the same premalignant stages in the response. It is intended, however, not to discover more facts; but, on the basis of the facts observed on the first level, to organize and carry out experiments designed to prevent the malignant change from taking place in tissue sufficiently exposed to the carcinogen otherwise to produce cancer. First, one would try every possible device of holding the reacting epidermis in the previous normal equilibrium and of counteracting the decreases in calcium, iron and other substances which give character to the new precancerous equilibrium. The swelling of cytoplasm and of nuclei and the evidence for decreased intranuclear viscosity suggest the advisability of exposing the epidermis to strongly hypertonic solutions despite the lack of chemical data pointing to increase in water content. But one should try all influences likely to affect epidermis in any way consistent with continued life of the animals, for unexpected factors may achieve the desired results. Those which accelerate the malignant transformation, such as injections of estradiol benzoate, are not to be neglected because they may serve as clues to inhibitors. While the first level obviously is fact-finding, the second is therefore one of purposeful control.

On the third level comes more fact-finding investi-

gation now of the chemical equilibrium of the resulting cancer and of all other possibly significant properties. Here we have made considerable progress; but much remains to be done, and the chances of expansion by adding other unit projects, as parts of the whole, are almost unlimited.

And on the fourth, or highest level, are purposeful efforts based on knowledge of the equilibrium in the cancer to disturb it and cure the cancer, and also to determine the specific vulnerability of the cancer cells by bringing to bear on them influences of wide variety, for again an unexpected agent may prove to be most effective. To concentrate on the first and third levels requires restraint bolstered by the belief that so doing will pay in the long run.

At all four levels, whether of fact-finding or of control, so many opportunities unfold that it requires no stretch of the imagination to see how at least 100 workers could profitably be employed, all integrated through investigation of the same biological equation by quantitative methods so that the results will all stack up. Our project is not unique in this regard. It is not difficult to think of others which can likewise be organized in such a way as fully to justify an almost wholesale approach.

What is needed is for the public to shed its colossal complacency concerning cancer and to insist on research being carried on as an "essential" activity, dominated by the spirit of *must*, not being shocked by the *cost*, which has achieved wonders in the war. The least we can do is to support the National Campaign of the American Cancer Society and to let our Senators and Representatives in Washington know that we confidently look to them to support the plans of the U. S. Public Health Service for Cancer Research.

OBITUARY

MAX BERGMANN
1886–1944

MAX BERGMANN, member of the Rockefeller Institute for Medical Research, died in New York on November 7, 1944, in his fifty-ninth year and at the height of his powers as an investigator in the field of organic biochemistry.

Born in Fuerth, Bavaria, on February 12, 1886, Bergmann received his college training in Munich. Like several other distinguished biochemists, he approached chemistry through the biological sciences. His original inclination had been towards botany, but in his early studies he was so much impressed by the need for chemical answers to botanical questions that he decided to acquire a fundamental training in organic chemistry. To this end he enrolled in the chemical department of the University of Berlin, then under the leadership of Emil Fischer; there he graduated in 1911, the work for his dissertation, on acyl polysulfides, having been directed by Ignaz Bloch. He then joined Fischer's group of collaborators in the investigation of amino acids and carbohydrates.

With the outbreak of war in 1914 Bergmann was selected by his chief as confidential scientific assistant, an appointment which brought with it exemption from military service. During the subsequent five years he was thus closely associated with all of Emil Fischer's research activities, which included not only the topics mentioned above, but the investigations of tannins and polyhydroxylic phenols. Among the important publications that bear Bergmann's name during that period are reports on the acylation of polyhydroxylic compounds partially protected by combination with acetone, on the synthesis of glucosides of gallic acid and mandelonitrile, on new methods for the preparation of α-monoglycerides and on the chemistry of glucal. After Fischer's death Bergmann almost automatically became his scientific executor, assuming the responsibility for the completion and publication of unfinished researches.

In 1921 he was appointed to the Kaiser Wilhelm Institut für Lederforschung in Dresden, where he continued his investigations in the field of carbohydrates and initiated his studies of the synthesis of unsymmetrical glycerides. A logical extension of this work to amino alcohols led on the one hand to the recognition of the migration of acyl groups and on the other to his abiding interest in amino acids and peptides.

Bergmann's duties in Dresden comprised, besides academic research, chemical studies of leather and tanning processes, and he was obliged to spend a large part of his time in consultation with industrialists. In view of the extensive traveling involved in this phase of his activities, his scientific productivity through the following decade was truly remarkable. Among the major problems which he attacked during this period was the general theory of the structure of polysaccharides and proteins. In 1925 he published his first papers on the chemistry of diketopiperazines derived from serine and cystine, with the aid of which he established a general method for the preparation of derivatives of dehydro amino acids. In the following year he first exploited the useful properties of azlactones for the synthesis of dipeptides, particularly those of phenylalanine, which he produced by the condensation of benzaldehyde and oxazolone with subsequent hydrogenation and con-

densation with other amino acids. Of unusual interest was his demonstration of the transference of the acylated amidine group of triacetyl arginine to the nitrogen atom of amino compounds, a process which could later be adduced as an analogue to the metabolic mechanism whereby urea is formed. A synthesis of creatine was devised on the basis of this reaction.

In the course of his work on amino acids and peptides, in which Bergmann was joined in 1927 by Zervas, the useful process for the racemization of amino acids by means of acetic anhydride was discovered. The mechanism of this reaction, at first obscure, was several years later elucidated by du Vigneaud, who in 1929 collaborated with Bergmann on the synthesis of tyrosylarginine and in a study of acyl migration from diacyl diketopiperazines to amino acids.

At the same time, investigations fundamental to carbohydrate chemistry were continued; the reactions of glucal were further explored and its pyranoid constitution was established. Bergmann also attacked the difficult problem of the intermediate products in the hydrolysis of cellulose and starch. Amino acids, however, occupied the center of the stage. It was shown that acylation of amino acids by ketene can proceed satisfactorily in aqueous solution. In 1930 an extended study of the action of proteolytic enzymes upon peptides of dehydro amino acids was undertaken, and Bergmann demonstrated the presence in pancreas and in yeast of enzymes which split glycyl dehydrophenylalanine into glycine and phenylpyruvic acid. With Grafe he developed an essentially converse synthesis of peptides of dehydroalanine from pyruvic acid. A characteristic example of Bergmann's chemical ingenuity is his application to glucosaminic acid of the information which he had gained in his studies of dehydro amino acids.

In 1932 Bergmann developed the carbobenzoxy method for the protection of amino groups during the synthesis of peptides. This was immediately adopted as standard practice by other workers; being as versatile as it is elegant, it has become one of the most effective weapons in the armamentarium of the amino acid chemist. More than any other device it helped to make possible the synthesis of the many types of peptide which Bergmann later employed as models in his classic studies of enzyme specificity.

In 1933 political and social conditions in Germany had reached a stage at which no self-respecting and sensitive Jew could continue to serve his State in a post of responsibility. As Bergmann arrived in this country without prior plan, New York, his port of entry, could take the opportunity to capture him for its own. The Rockefeller Institute provided him with an associate membership and generous working facilities; three years later, on the retirement of the late Phoebus A. Levene, Bergmann became a member of the institute and the head of the laboratory of chemistry, a position which he held until his death.

The last scientific report to be written in the Dresden laboratory dealt with the mode of linkage of proline in gelatin, in which the existence of peptide bonds involving the nitrogen of proline was demonstrated. With characteristic delicacy of sentiment, Bergmann continued to publish in German journals the results of researches carried out in Germany. These were of high importance, for in them he laid the foundations of his studies of the specificity of proteolytic enzymes. His views on the subject are set forth in the published forms of lectures delivered before the Rockefeller Institute, the American Leather Chemists' Association and the Harvey Society. His exploration of this field was continued unremittingly in New York with the collaboration at first of Zervas, who had followed him from Dresden, and later of his younger American colleagues Fruton, Ross and Behrens. These investigations, in which his powers of experimentation and imaginative interpretation reached their zenith, culminated in the theories, developed with Fruton, of the specificity of proteinases and the relation of structure to kinetics of enzyme action.

Bergmann's demonstration of the ability of a proteolytic enzyme to effect the synthesis of peptides and the redistribution of peptide bonds between substrates carried far-reaching implications with respect to the intermediary metabolism of proteins, and it led him to advance the hypothesis that the structural pattern of a protein, in all its details, is a consequence of the specificity of the intracellular proteinases. His suggestion that in living organisms the synthetic reactions incident to protein formation are made possible through the coupling of proteolytic systems with other equilibrium systems by means of which the synthetic products are removed from the zones of degradative activity is likely to have a profound effect on biochemical thought.

It was natural that his constant preoccupation with theories of proteolysis and protein synthesis should have involved Bergmann in speculation as to the structure of proteins. In order to attack the fundamental problem of the order in which the constituent amino acids are arranged in a polypeptide chain he devised, with Zervas, an elegant procedure for stepwise degradation which started at the free carboxyl group and permitted the identification of each successive component. However, exploitation of the possibilities inherent in this technique had to await the realization of pure peptide fragments of proteins. He therefore approached the problem from a more theoretical standpoint. From analytical data secured largely by methods developed by himself he calculated

that in gelatin every third amino acid could be glycine, every sixth proline, and every ninth hydroxyproline. This finding led him to postulate a systematic periodicity in the location of these amino acids in the peptide chain. With Niemann he extended the application of this concept to a wider series of amino acids in other proteins, and advanced the general hypothesis that the individual amino acids are situated in proteins in regularly recurrent orders dependent on periodicities the numerical values of which are multiples of powers of 2 and 3. Though later evidence suggests that this hypothesis represents an oversimplification, the basic idea has stimulated many useful studies, not the least of which has been the development in Bergmann's own laboratory of precise methods, novel in principle, for the analytical determination of amino acids for which no reliable procedures had previously been available.

Max Bergmann possessed in a high degree the capacity for forming and maintaining affectionate friendships. He was incapable of malice, and never displayed rancor towards those who had wrecked his career in his native land. He was gifted with an inextinguishable fund of quiet humor, he was invariably generous towards younger men and towards the scientific work of his colleagues, and his innate modesty was never clouded by his objective though unexpressed recognition of the value of his own achievements.

He is survived by his wife, a son and a daughter.

HANS T. CLARKE

COLUMBIA UNIVERSITY

DEATHS AND MEMORIALS

DR. ROBERT H. MACKNIGHT, research associate in biology at the University of Rochester, died on August 3. He was twenty-nine years old.

GEORGE WILLETT, since 1928 curator of ornithology at the Los Angeles County Museum, died on August 2 at the age of sixty-six years. He had been connected with the museum since 1927. He was vice-president of the American Ornithological Union and secretary of the Cooper Ornithological Club, Inc.

DR. E. HADORN, professor of zoology at the University of Zurich, Switzerland, has written to Dr. Curt Stern, of the University of Rochester, that the following German zoologists have been killed in action: E. Ries, E. Becker and W. Köhler.

A TABLET to commemorate the work of the late Sir William Bragg, O.M., and of his son, Professor Sir Lawrence Bragg, presented by Mrs. Smithells, the widow of Professor Arthur Smithells, of the University of Leeds, was unveiled on July 20 by Professor R. Whiddington, F.R.S. The inscription on the tablet reads: "Near this place in the old Physics Laboratory in the year 1913 William Henry Bragg, Cavendish professor of physics in this university from 1909 to 1915, and his son, William Lawrence Bragg, began their joint researches and established with the first x-ray spectrometer the nature of x-ray spectra and the principles of crystal analysis for which they were awarded the Nobel Prize in 1915."

SCIENTIFIC EVENTS

SCIENCE IN DENMARK AND NORWAY

THE scientific correspondent of *The Times*, London, reports that the Royal Society is taking a very active part in renewing the cordial relations which have by long tradition existed between men of science of Great Britain and of the lands recently liberated from Germany. In this connection Professor A. V. Hill has paid a visit to Denmark and Norway. *The Times* describes his visit as follows:

He went as the delegate of the society, to bear its greetings, to present to the academies of the two countries copies of all that the Royal Society has published since 1940, and to request the academies to be instrumental in distributing to scientific workers of their respective countries certain sums of money from a fund founded, in memory of Sir Horace Darwin, for the purchase of scientific instruments.

He received a most cordial and sincere welcome at Copenhagen and at Oslo, and has returned with the greatest admiration for the spirit that he found abroad, and with high hopes for the future of Danish and Norwegian science.

Science in Denmark has not suffered as badly as in most countries occupied by the Germans. Until the autumn of 1943 the invaders were on their best behavior, but at that time the *Gestapo* became active and students ceased to attend the colleges. Professor Rehberg, the zoologist, was brutally mishandled by the Germans for lack of cooperation, and he and a good many other men of science were imprisoned, but escaped when the prison was very skillfully bombed by us. Research, however, continued in the laboratories which were not despoiled, and much excellent work has been published in the *Proceedings* of the academy.

Food is in good supply and the generous Danes have done and are doing sterling work in collecting food for Norway and Holland. Their chief scientific need is books and journals, and English text-books for students. To show how quickly the Danes have been able to establish themselves, they are contemplating an expedition next year for marine biological investigation, a subject in

which they have high traditions, off the west coast of Africa. They already have a ship and funds. They trust that our authorities will facilitate the work, in which they will gladly welcome the aid of the British biologists.

Norway has suffered much more than Denmark. The president of the academy, Professor Bull, was three years in a concentration camp: the scientific laboratories have been stripped of apparatus and the departments closed. In consequence, little scientific work has been carried out during the war and the Norwegians are having great difficulty in getting their courses started again. Medicine in Norway attained, before the war, a very high standard, and it is most desirable that medical instruction should get under way as soon as possible. The Danes are taking a large number of Norwegian medical students, and Norway is anxious that some of her best post-graduate students should study in England. These men are ready to come now and there are very real reasons why we should help. Norway's geologists are anxious to serve for a period in our surveys abroad and her oceanographers and biologists would gladly take part in our expeditions.

THE OFFICE OF RESEARCH AND INVENTIONS OF THE NAVY DEPARTMENT

THERE is given in *Chemical and Engineering News* an account of the new Office of Research and Inventions to guide navy research activities, which has been established by the Navy Department, under the direct supervision of the Secretary of the Navy. The office was formed by merging the Naval Research Laboratory, the Special Devices Division of the Bureau of Aeronautics, the Office of Research and Development and the Office of Patents and Inventions.

Rear Admiral Harold G. Bowen, U.S.N., who was director of the Office of Patents and Inventions, and was associated with the development of radar and high-pressure, high-temperature steam propulsion for naval vessels, has been placed at the head of the new office. Captain Luis de Florez, U.S.N.R., director of the Special Devices Division of the Bureau of Aeronautics and winner of the Collier trophy in 1944, will be assistant chief.

The office is authorized by the Secretary of the Navy and Chief of Naval Operations to continue and to instigate such experimentation as is necessary to maintain the superiority of American naval weapons. It will assist in the adaptation to naval needs of jet propulsion, rockets, gas turbines and numerous weapons and techniques still in a secret category and will deal with all chemical engineering projects for the Navy.

STUDY OF THE CAUSES AND TREATMENT OF CANCER

AT a press conference on August 7, presided over by Alfred P. Sloan, Jr., chairman of the General Motors Corporation, it was announced that the Alfred P. Sloan Foundation had made, for a ten-year study of the causes and treatment of cancer, a grant of $4,000,000 to Memorial Hospital for the Treatment of Cancer and Allied Diseases, which will now become an international center for the study of the disease.

Participating in the conference were Dr. Charles F. Kettering, president of the American Association for the Advancement of Science, vice-president and director of research of the General Motors Company; Reginal G. Coombre, president of the hospital, and Dr. C. P. Rhoads, director of the hospital.

The gift in connection with the recently announced expansion program of Memorial Hospital will provide for a building especially designed for the purpose, self-contained in all its various research functions. It will be erected at an estimated cost of $2,000,000 on property now owned by Memorial Hospital adjacent to its present location.

In addition, the Alfred P. Sloan Foundation will undertake to provide $200,000 a year toward the operating cost for a definite period of ten years. This is estimated to be not more than half of what might be profitably employed. It is to be hoped that others interested in the same objective will provide additional financial support.

The Sloan-Kettering Institute building will stand in the middle of Memorial Cancer Center. It will be conducted by a separate Board of Trustees composed of men primarily interested in research, and the funds entrusted to the charge of these trustees will be used for no other purpose than for research. As an integral part of the center, however, all the clinical facilities and material of the other units of the center will be available to the institute.

While the gift provides for most of the financial requirements of the research phase of Memorial Cancer Center, it will not be fully effective from the point of view of its ability to render service until it is completed. This will necessitate approximately $3,000,000 to $4,000,000 in addition. These additional funds will provide for an increased bed capacity at Memorial Hospital proper, for fellowships for the training of specialized medical personnel and for equipment necessary to the servicing of the new James Ewing 300-bed unit to be erected at the center by the City of New York. When this program has been completed, there will be no comparable center wholly devoted to the cause of cancer, and so fully integrated, existing anywhere in the world.

A separate board of trustees will supervise the institute. There will be four representatives of the foundation and five of the hospital.

The Cancer Center will be a unit of a group of institutions for medical care, teaching and research.

This group includes the New York Hospital, Cornell University Medical College, with which Memorial Hospital is affiliated, and the Rockefeller Institute for Medical Research.

THE INSTITUTE OF NUCLEAR STUDIES AND THE INSTITUTE OF METALS AT THE UNIVERSITY OF CHICAGO

IT is planned to establish at the University of Chicago an Institute of Nuclear Studies and an Institute of Metals. Dr. Samuel K. Atkinson, professor of physics, will serve as the director of the Institute of Nuclear Studies.

Dr. Enrico Fermi and Dr. Harold Urey, both of Columbia University, have been appointed professor of physics and professor of chemistry, respectively. Members of the institute will include Dr. Philip W. Schutz, professor of chemical engineering, Columbia University; Dr. Edward Teller, professor of chemistry, George Washington University; Dr. Joseph E. Mayer, professor of chemistry, Columbia University, with his wife, Maria Goeppert Mayer, who will serve as research associate; Dr. Walter H. Zinn, associate professor of physics now in war research in Chicago, and Dr. John Simpson, Dr. Robert F. Christy and Dr. Donald J. Hughes, all of the University of Chicago.

The staff of the Institute of Metals will consist of Dr. Cyril Stanley Smith, director, and Dr. Clarence Zener, professor of metallurgy.

SCIENTIFIC NOTES AND NEWS

THE University of Southern California, Los Angeles, conferred on June 23 the honorary degree of doctor of science on Dr. Walter L. Treadway, Los Angeles, formerly assistant surgeon general of the U. S. Public Health Service.

THE degree of doctor of laws of Queens University, Ontario, Canada, has been conferred on Dr. Walter R. Bloor, professor of biochemistry at the School of Medicine and Dentistry of the University of Rochester.

DR. ALBERT D. KAISER, professor of child hygiene at the School of Medicine of the University of Rochester, was recently awarded the Rochester Civic Medal by the Rochester Museum Association. Dr. Kaiser has also been elected for a three-year term to the Board of Trustees of the Rochester Academy of Medicine.

THE Government of Panama has conferred upon Dr. J. C. Geiger the decoration of the Orden de Vasco-Nunez de Balboa, grade of Knight Commander. This is granted with the same citation as previously bestowed by Panama in 1942: "For distinguished, distinctive and generous services in public health given over a long period of time to the residents from Panama and to Panama, and a living example of the perpetuation and enrichment of Pan Americanism."

DR. CORNELIA T. SNELL, of Brooklyn, has been elected chairman of the New York Section of the American Chemical Society.

DR. C. E. GORDON, professor of geology and mineralogy at the Massachusetts State College, has resigned as chairman of the division of science, a position that he has held since 1927.

DR. ARTHUR P. WYSS, head of the department of pharmacy of the University of Buffalo, has been appointed dean of the School of Pharmacy at Western Reserve University.

LIEUTENANT COLONEL HARDY A. KEMP, M.C., A.U.S., was recently named dean of the College of Medicine of Wayne University, Detroit. Since his return from two years service over-seas which included duty in the West Indies, British and French West Africa and India, he has been secretary of the Army Medical School in Washington, D. C. At the time of his return he was deputy theater surgeon for the China-Burma-India Theater. Prior to his taking active duty in February, 1942, Colonel Kemp was formerly dean of the Medical College and director of the University Hospital of the Ohio State University.

DR. WILFRED W. WESTERFELD, associate in biochemistry at the Harvard Medical School, Boston, has been appointed professor of physiology at the College of Medicine of Syracuse University.

DR. CARL G. HELLER, assistant professor of physiology at the College of Medicine of Wayne University, has been appointed associate professor of physiology and medicine at the School of Medicine of the University of Oregon.

DR. A. GLENN RICHARDS, JR., assistant professor of zoology at the University of Pennsylvania, has been appointed associate professor in the Division of Entomology and Economic Zoology of the University of Minnesota to teach and direct graduate research in insect physiology and insecticides.

DR. EDWARD P. CLAUS, formerly of the University of Pittsburgh, has been appointed assistant professor of botany and pharmacognosy at the College of Pharmacy of the University of Illinois. During the 1944-45 term he taught at the College of Pharmacy, University of Puerto Rico.

THE College of Medicine of the University of Tennessee announces the following promotions and new appointments: Dr. S. R. Bruesch and Dr. Frank Harrison have been promoted from assistant professorships to associate professorships of anatomy; Dr. Francis Murphey from assistant professor to associate professor of neurosurgery; Dr. James R. Reinberger from associate professor to professor of obstetrics and gynecology, and Dr. R. O. Rychener from assistant professor to associate professor of ophthalmology. Dr. Frank E. Whitacre has been promoted from associate professor to professor of obstetrics and gynecology, and has been made chief of the division. Dr. I. N. Dubin, of Duke University, has been appointed assistant professor of pathology and bacteriology; Dr. John Hunter becomes instructor in physiology, and Dr. Hugo Krueger, associate professor of pharmacology.

DR. A. C. HARDY, of Exeter College, has been appointed to the Linacre professorship of zoology and comparative anatomy at the University of Oxford from such date, not being later than January 1, 1946, as he can assume the work.

DR. NATHAN FASTEN, who recently resigned as professor and head of the department of zoology at Oregon State College, has been appointed chief biologist for the State of Washington Pollution Control Commission. His office is in Bagley Hall, University of Washington, Seattle, Wash.

WALLACE E. PATT, petroleum geologist, has retired as a director and member of the executive committee of the Standard Oil Company of New Jersey.

DR. IRVING H. BLAKE, professor of zoology at the University of Nebraska, has been granted leave of absence for the fall semester in order to continue his ecological research on "A Seasonal Study of the Animal Communities of Mt. Lincoln, Colo.," which he has been carrying on during the summers in the Rocky Mountains.

THE Federation of British Industries, of which Dr. B. J. A. Bard, chemist, is chief of the executive staff, has voted to establish a special research committee to maintain close liaison between industry and science. A committee of twenty members presided over by Sir William Larke has been appointed. The chief objectives of the group are to maintain contact between British companies and research organizations to encourage British industry to extend its research facilities and to see that the results of research are utilized to the fullest. A two-day conference on "Industry and Research" is planned in London, at which special emphasis will be laid on the practical means by which research can assist industry and promote industrial efficiency, exports, full employment and a higher standard of living.

THE Gerontological Society, Inc., an outgrowth of the American Division of the Club for Research on Ageing, founded in 1939, plans to establish *The Journal of Gerontology,* to be issued quarterly beginning during the first quarter of 1946. The Committee on Publications consists of Dr. Roy G. Hoskins, Harvard Medical School, *chairman;* Lawrence K. Frank, New York; Dr. William de B. MacNider, University of North Carolina, and Dr. Edward J. Stieglitz, Washington, D. C. The editor-in-chief is Dr. Robert A. Moore, Washington University School of Medicine, St. Louis.

DR. WM. RANDOLPH TAYLOR, of the University of Michigan, writes to SCIENCE that a card received from Professor Paul van Oye of Ghent, student of the freshwater algae of Belgium and its possessions, indicates that he is well and apparently has been able to continue scientific work during the war. Professor A. Conard wrote indicating that the *Jardin expérimental Jean Massart* at Brussels, and its collections, had suffered little during the German occupation. Professor Conard has returned to his work at the experimental gardens. A letter from Dr. Josephine Th. Koster, phycologist and assistant in the Rijksherbarium, Leiden, indicates that that institute, its staff and collections, survived the German occupation without loss.

PROFESSOR AUSTIN M. PATTERSON, of Antioch College, writes to SCIENCE that Dr. W. P. Jorissen, Hooge Rijndijk 15, Leiden, Holland, editor of *Chemisch Weekblad* and *Recueil des travaux chimiques des Pays-Bas,* reports that the Dutch need American chemical literature, and he hopes that American colleagues will send reprints of their publications during the last six years. Review copies of new books will of course be very welcome. Dr. Jorissen offers to arrange for the distribution of books and reprints which may reach him. He and his family are recovering from malnutrition due to insufficient food.

THE officers, executive committee and members of the Division of Geology and Geography of the National Research Council, for the year beginning on July 1, 1945, are as follows: *Chairman,* William W. Rubey; *Vice-chairman,* Lester E. Klimm; *Executive Committee,* William W. Rubey, Lester E. Klimm, Charles H. Behre, Jr., Monroe G. Cheney, Otto E. Guthe, Marshall Kay; *Representatives of Societies,* Marland Billings and Marshall Kay, Geological Society of America; J. F. Schairer, Mineralogical Society of America; L. W. Stephenson, Paleontological Society; Otto E. Guthe and Glenn T. Trewartha, As-

sociation of American Geographers; Raye R. Platt, American Geographical Society; Charles H. Behre, Jr., Society of Economic Geologists; Monroe G. Cheney, American Association of Petroleum Geologists; L. H. Adams, American Ceramic Society; John A. Fleming, American Geophysical Union; *Representative of the Government designated by the President of the United States,* W. E. Wrather; *Members at Large,* W. Storrs Cole, Lester E. Klimm and William W. Rubey.

SPECIAL ARTICLES

THE *IN VITRO* PROTECTION OF PENICILLIN FROM INACTIVATION BY PENICILLINASE

RECENTLY the authors reported a method for the production of an anti-penicillinase immune serum.[1] As readily as the acquisition of immune sera would permit, the investigations were extended to evaluate the therapeutic utilization of such a preparation.

Chow and McKee[2] demonstrated the delayed action of penicillin by combining it with human plasma proteins. They further state that this penicillin-albumin complex, unlike the sulfonamide-albumin complex believed not to possess bacteriostatic activity,[3] does demonstrate antibiotic activity. It was therefore believed that a penicillin-immune plasma protein complex would possess bacteriostatic activity and what is probably more important, also offer protection to the penicillin from destruction by penicillinase.

EXPERIMENTAL

Normal rabbit serum and penicillinase immune rabbit serum were added in varying amounts to a solution containing 4,000 units of penicillin. The volume was restored to 2 cc and after 6 hours' contact, with occasional shaking at 5° C, penicillinase (purity-380 units/mgm) was added in varying amounts, the volume restored to 5 cc, shaken well and incubated at 37° C for one hour. The samples were removed, cooled in an ice bath and immediately assayed by the agar cup plate method.

TABLE 1

	Serum volume (ml)	Penicillinase units	Penicillin (Oxford units)	Activity (after 1 hour)
Normal serum	0.25	5	4,000	+
	0.25	10	"	+
	0.25	15	"	+
	0.25	20	"	+
	0.25	25	"	0
	0.25	30	"	0
	0.5	5	"	+
	0.5	10	"	+
	0.5	15	"	+
	0.5	20	"	+
	0.5	25	"	0
	0.5	30	"	0
Immune serum	0.25	70	"	+
	0.25	80	"	+
	0.25	90	"	+
	0.25	100	"	+
	0.25	110	"	0
	0.5	80	"	+
	0.5	90	"	+
	0.5	100	"	+
	0.5	110	"	+
	0.5	120	"	0

[1] D. Perlstein and A. J. Liebmann, SCIENCE, this journal.

[2] B. C. Chow and C. M. McKee, SCIENCE, 101: 67, 1945.

[3] B. D. Davis, SCIENCE, 95: 78, 1942.

Experiments were made at two levels of penicillin, with a more pronounced effect at the lower level.

It was found that under the conditions of the experiments, 4,000 units of penicillin were protected from inactivation by as high as 100 units of penicillinase through the addition of 0.25 cc of immune serum. In the control series with normal serum or saline no protection was afforded and less than 25 units of penicillinase were needed for complete inactivation of the penicillin in one hour at 37° C.

TABLE 2

	Serum volume (ml)	Penicillinase units*	Penicillin (Oxford units)	Activity (after 1 hour)
Normal serum	0.25	1	1,000	+
	"	3	"	+
	"	5	"	0
	"	7	"	0
	"	9	"	0
	"	11	"	0
Immune serum	"	25	"	+
	"	30	"	+
	"	35	"	+
	"	40	"	+
	"	45	"	+
	"	50	"	+
	"	55	"	0
	"	60	"	0

* A unit of penicillin[4] is that amount of enzyme which in 11 ml of pH 7.0 solution containing 50 Oxford units of penicillin will destroy in one hour at 37° C an amount of penicillin equal to 57.5 per cent. of the penicillin recovered in the control.

In Table 2 it will be noted that the protective effect of immune sera for penicillin is exaggerated by the use of less penicillin (1,000 units instead of 4,000 units) under the same test conditions. It was found that 1,000 units of penicillin was protected from inactivation by as high as 50 units of penicillinase through the addition of 0.25 cc of immune serum, whereas in the control series with normal serum less than 5 units of penicillinase was required for complete inactivation of the penicillin in one hour at 37° C.

It is not known whether a true chemical compound is formed by the addition of penicillin to immune plasma protein, but should this be the case, there would result not only a slower excretion of this com-

[4] E. B. McQuarrie, A. J. Liebmann, R. G. Kluener and A. T. Venosa, *Archiv. Biochem.*, 5: 307, 1944.

pound from the animal body due to its increase in molecular weight, but in addition the protective effect of the immune sera to counteract the destructive action of penicillinase normally present in the animal body. It is believed that this is an entirely new approach to the important problem of the delayed action of penicillin. Studies are now in progress along this line and will be published at a later date.

SUMMARY

(1) A combination of penicillin and immune plasma protein has been obtained which possesses bacteriostatic activity.

(2) The presence of the penicillinase immune plasma protein in this mixture protects penicillin *in vitro* from destruction by penicillinase.

Acknowledgments: The authors wish to express their appreciation to I. Dorrell and D. Klingelhoffer for their technical assistance.

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THE EFFECT OF THIOURACIL ON THE RESPIRATION OF BONE MARROW AND LEUCOCYTES *IN VITRO*

THE widespread use of thiouracil in the treatment of hyperthyroidism carries with it the hazard that serious leucopenia or even fatal agranulocytosis may occasionally occur suddenly and unexpectedly during the course of therapy. This danger was pointed out in Astwood's original paper[1] and has been amply confirmed by subsequent reports.[2] It consequently seemed desirable to determine whether thiouracil has any demonstrable effect on the respiratory metabolism of the bone marrow of an experimental animal and to investigate the possibility of combating any depressant action which might be found.

Rabbit femoral bone marrow was employed, the techniques for handling this tissue for measurement of respiration in the Warburg apparatus having been previously worked out.[3] The medium used was autogenous partially neutralized serum, with and without added thiouracil in final concentration of 100 mg per cent. This concentration is much higher than that in the serum of patients being treated with the drug, but it has been shown[4] that in persons receiving thiouracil in therapeutic amounts the drug is highly concentrated in the bone marrow, reaching levels comparable with the above. Most of the determinations were made in triplicate, the others in duplicate. The results reported below are based on the rates of respiration found during the third hour of 3-hour experiments. Differences of ±5 per cent. between the average rates of respiration of the control samples and those in presence of thiouracil were interpreted as being within the limits of experimental error. Marrows of various cellular composition were obtained by injecting the animals from 3 to 12 days earlier with (a) acetylphenylhydrazine intraperitoneally to produce erythroid metaplasia, or (b) croton oil intrapleurally[5] to produce myeloid metaplasia, previous experience having indicated that neither of these drugs affects the respiratory metabolism of the marrow cells. In each experiment, the proportion of myeloid and erythroid cells present was determined by making differential cell counts on marrow smears stained with Wright-Giemsa.

The results have been found to depend largely upon the cellular composition of the marrow. Of 10 predominantly erythroid marrows (< 40 per cent. myeloid cells) only 3, or 33 per cent., showed a small depression of respiration averaging 9 per cent. ±2.3 per cent. in the presence of thiouracil. Of 13 marrows in an intermediate group (composition between 40 per cent. and 60 per cent. myeloid cells) 5, or 38 per cent., showed a depression of respiration averaging 10 per cent. ±1.0 per cent., while of 14 predominantly myeloid marrows (> 40 per cent. myeloid cells) 13, or 93 per cent., showed a depression of respiration that averaged 13 per cent. ±1.3 per cent. This more uniform and slightly greater susceptibility of the myeloid cells to the depressant effect of thiouracil on cellular respiration led us to determine the effect of the drug on the cells of rabbit peritoneal exudates, since these are virtually all polymorphonuclear leucocytes.[6] In each of 4 experiments in which these cells were washed and resuspended in the same type of media used for the marrow experiments, thiouracil was found to depress respiration, but the extent of the depression (12.9 per cent. ± 1.1 per cent.) was almost identical with that found in "predominantly myeloid" marrows described above. The cell counts of these marrows averaged only 66 per cent. myeloid cells, and since the remaining erythroid cells have been shown to be considerably less susceptible to the action of the drug, the inference is that myeloid marrow cells (mostly myelocytes) are more sensitive to the action of the drug than the mature polymorphonuclear cells found in exudates. Direct

[1] E. B. Astwood, *Jour. Am. Med. Asn.*, 122: 78, 1943.
[2] J. Kahn and R. P. Stock, *ibid.*, 126: 358, 1944; I. Ferrer, D. N. Spain and R. T. Cathcart, *ibid.*, 127: 646, 1945; S. L. Gargill and M. F. Lesses, *ibid.*, 127: 890, 1945.
[3] C. O. Warren, *Am. Jour. Physiol.*, 128: 455, 1940; *ibid.*, 131: 176, 1940; *Jour. Biol. Chem.*, 156: 559, 1944.
[4] R. H. Williams, G. A. Kay and B. J. Jandorf, *Jour. Clin. Inv.*, 23: 613, 1944.
[5] C. O. Warren, *Cancer Research*, 3: 621, 1943.
[6] E. Ponder and J. MacLeod, *Jour. Exp. Med.*, 67: 839, 1938.

observations were also made, on a warmed microscope stage, of the motility of the exudate cells and the myelocytes in the marrow. Thiouracil in 100 mg per cent. concentration did not appear to affect the motility of either type of cell.

Finally, 13 attempts to protect the marrow and exudate cells from the depressant action of thiouracil on respiration by adding 10 mg per cent. pyridoxine[7] *in vitro* all yielded negative results, as have 4 preliminary experiments with diluted liver extract.

A detailed account of these experiments will be published elsewhere.

Summary and Conclusions

Thiouracil in 100 mg per cent. concentration induces a small but significant inhibition of respiration of rabbit bone marrow cells, the effect upon the myeloid elements being the more striking. By comparing the results with those obtained with the polymorphonuclear cells of rabbit peritoneal exudates, it is inferred that the more immature marrow cells are more seriously affected. No effects on cell motility have been observed, and attempts to oppose the effect of thiouracil with pyridoxine have been unsuccessful. While caution must necessarily be exercised in relating the results of the present *in vitro* experiments to the known toxic effects of thiouracil in patients, the methods outlined above might be employed to test possible toxic effects of new therapeutic drugs, or the action of agents proposed to protect the marrow from harmful effects.

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ANTAGONISTIC ACTION OF A RED MOULD PIGMENT AGAINST BACTERIA OF THE TYPHOID-PARATYPHOID-DYSENTERY GROUP

A mould which produces a red pigment was isolated in our laboratory from human hair planted on Sabouraud's agar.

The mould grows rapidly at room temperature, spreading within 3 to 4 days over the whole surface of an agar plate. At first, the colony is fluffy and pure white; later, within 2 to 3 weeks, it becomes slightly yellowish. A striking characteristic of the mould is the production of a dark red pigment readily diffusing in the medium. No fruiting structures were observed regardless of medium or conditions of growth. The absence of these structures made impossible the identification of the mould.[1] However, it bears no resemblance to any of the known pathogenic fungi. Essential for the formation of the pigment is an organic source of nitrogen (peptone, proteose, casein, bran) and the presence of one of the sugars (dextrose, sucrose, maltose). No pigment is formed on media containing lactose or starch or on Czapek-Dox medium which is used for Penicillium cultures and contains inorganic nitrogen compound. The following medium gives a satisfactory production of pigment: Proteose 1.0, Dextrose 4.0, Agar 0.25, Water 100.0.

The medium is distributed in flasks or bottles in shallow layers 1.5 to 2 cm deep. Three or four days after inoculation, a compact white felt of mycelium develops on the surface of the medium. The formation of pigment which diffuses in the medium begins on the second or third day and attains its peak about the eighth to the tenth day. The pigment can be extracted from the medium by the method used in production of penicillin. After acidification with phosphoric or hydrochloric acid to pH2 the culture medium is shaken with an equal volume of an organic solvent, like ether, amylacetate, butyl alcohol, chloroform. From this solvent the pigment is reextracted by shaking with a phosphate buffer solution of pH7.

The activity of the pigment solution was tested by the Oxford cup method. When typhoid, paratyphoid or dysentery (strains of Shiga and Flexner) bacilli not susceptible to the action of penicillin were seeded on agar plates there always appeared a clear zone of complete inhibition of growth around the cup placed on the surface of agar and filled with the pigment solution. The diameter of the clear zone was 20 to 30 mm. On the other hand, gram-positive bacteria, sensitive to penicillin, such as staphylococci, streptococci, pneumococci and subtilis, were in no way affected by the pigment.

Cultures of the mould grown on media which did not produce pigment did not show antibiotic action—a finding which supports the assumption that the antibiotic properties are intimately connected with the pigment.

The pigment solution is stable and does not lose its antibiotic property after autoclaving, acidification (to pH2) or alkalinization (pH10).

After intravenous injection into a rabbit the pigment, within several minutes, appears in the urine from which it may be recovered in the usual way (acidification, extraction with organic solvent, reextraction with a buffer phosphate solution).

The pigment is not affected by the gastric secretion. When introduced by a tube into the stomach of a

[7] M. M. Cantor and J. W. Scott, Science, 100: 545, 1944.

[8] These studies were aided by a grant from the John and Mary R. Markle Foundation.

[1] This fact was confirmed by Dr. E. Muskatblit, of New York University, and by K. B. Raper, of the Northern Regional Research Laboratory, U. S. Department of Agriculture, to whom Dr. Muskatblit sent the culture for identification. To both I wish to express my gratitude.

rabbit the pigment within one hour can be demonstrated in the blood and urine.

Animal experiments are now under way to study the toxicity and effectiveness of this antibiotic.

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THE Rh AND Hr FACTORS IN CHIMPANZEES[1]

THE purpose of this paper is to report the results of tests for the Rh blood types and Hr factor on ten chimpanzees, three jungle-born and seven colony-born.

In the Rh and Hr tests,[2] the bloods of all ten chimpanzees behaved alike. In the tests for the Rh blood types, with sera anti-Rh_0, anti-Rh′ and anti-Rh″, the reactions were either negative or weak. When any agglutination occurred, this proved to be due to heteroagglutinins rather than specific Rh agglutinins, as was proved by absorption tests. Thus, absorption of the sera with chimpanzee blood removed the agglutinins for chimpanzee blood without affecting the reactivity of the serum for Rh-positive human blood; while absorption with human Rh-positive blood removed the agglutinins for human blood without affecting the reactions of the sera with chimpanzee blood. These results, therefore, indicate that all ten chimpanzees are Rh negative.

That this conclusion is correct was proved by tests for the Hr factor. In tests with an exceptionally potent anti-Hr serum it was found that the chimpanzee bloods were all agglutinated strongly and to the same titer of the serum (about 250) as human Rh-negative blood. Absorption with chimpanzee blood removed the agglutinin for human Rh-negative blood as well as the reaction for chimpanzee blood and, conversely, absorption with human Rh-negative blood destroyed the reactivity of the Hr serum for chimpanzee blood. Moreover, the anti-Hr agglutinin was absorbed equally well by equivalent volumes of chimpanzee and human Rh-negative red cells.

These investigations are being continued, and additional chimpanzees at the Yerkes Laboratories will be tested.* Most likely, the other chimpanzees will also give reactions corresponding to the human Rh-negative type. Perhaps this uniformity in the reactions of chimpanzee bloods is the final result of the selective action of isoimmunization in pregnancy, without the interference of racial crossing such as is apt to occur in man.[3]

[1] Aided by a grant from the United Hospital fund of New York City.

[2] For technique see: A. S. Wiener, J. P. Zepeda, E. B. Sonn and H. Polivka, *Jour. Exp. Med.*, 81: 559, 1945.

* After this article was submitted for publication, blood from five additional chimpanzees was tested, with similar results in the Rh and Hr tests.

[3] A. S. Wiener, SCIENCE, 96: 407, 1942.

In conclusion it should be mentioned that nine of the chimpanzees gave reactions corresponding to group A, while one gave reactions corresponding to group O. This agrees well with previous reports on a total of 92 chimpanzees, of which 81 belonged to group A and 11 to group 0.[4] The bloods of all ten chimpanzees reacted strongly with our anti-M serum, in conformity with the previous finding that all chimpanzees possess M-like agglutinogens.[5, 6] The anti-N serum which we had available did not agglutinate the chimpanzee bloods, but this does not necessarily contradict the conclusion from tests with other anti-N sera that chimpanzee blood also contains N-like agglutinogens.[6, 7]

The authors wish to express their appreciation to the staff of the Yerkes laboratories for their cooperation in obtaining the blood samples.

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ACCUMULATION OF DDT IN THE BODY FAT AND ITS APPEARANCE IN THE MILK OF DOGS[1]

THE high lipoid-water distribution ratio of DDT suggested that it might be preferentially stored in the adipose tissues of mammals fed DDT. The toxicological behavior of this compound pointed also to possible deposition in body fat. Such a preferential distribution was first indicated by feeding the dibrom analogue of DDT, 2,2-bis(p-bromophenyl)-1,1,1-trichloroethane, to rats and rabbits and determining the increase in tissue levels of bromine. The rise in the bromine content of the fat was many times that in the liver, kidney, brain or blood. These analyses, however, did not show the exact nature of the stored compound. It was not until the specific colorimetric method of Schechter and Haller[2] became available that the material stored in the fat was shown to be the unchanged DDT. The extent to which DDT will accumulate in the fat of chronically fed animals

[4] A. S. Wiener, "Blood Groups and Transfusion," 3rd edition, chapter XIX, C. C Thomas, Springfield, Ill., 1943.

[5] K. Landsteiner and P. Levine, *Jour. Exp. Med.*, 47: 771, 1928.

[6] A. S. Wiener, *Jour. Immunol.*, 34: 11, 1938.

[7] A. S. Wiener, *Am. Nat.*, 75: 199, 1943.

[1] A portion of the funds used in this investigation was supplied by a transfer, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the Division of Pharmacology of the Food and Drug Administration.

[2] M. S. Schechter and H. L. Haller, *Jour. Am. Chem. Soc.*, 66: 2129, 1944.

should be an important factor in the toxicological evaluation of this insecticide.

ACCUMULATION OF DDT IN THE BODY FAT

We had available for this study a number of dogs which had been receiving daily doses of DDT for periods of time varying from 138 days to two years. Since it was desired to continue the chronic experiments, these animals were anesthetized by intravenous injection of 40 mg/kg of sodium pentothal and samples of fat were taken from the peritoneal cavity under aseptic conditions.

The samples of fat were extracted with ether and the DDT determined by the Schechter and Haller[2] method. The quantities found in relation to dosage level, length of administration and form of dosage are shown in Table 1.

TABLE 1

ACCUMULATION OF DDT IN THE BODY FAT OF DOGS

Dog no.	Sex	Weight kg	Daily dose mg/kg	Form of administration	Days duration	DDT in fat mg/gm
M–166	f	8.9	10	soln.	747	0.080*
81–196	m	10.0	10	soln.	747	0.024
1–20	f	6.5	50	soln.	443	1.65
81–195	m	10.4	50	soln.	747	4.94
1–35	f	6.9	80	solid	443	0.39
M–171	m	10.3	80	solid	443	0.67
After discontinuing dose for 81 days						
1–59	f	7.3	80	soln.	138	0.013
1–61	m	9.3	80	soln.	138	0.00

* For purposes of comparison, the intravenous lethal dose of DDT is of the order of 0.04 milligrams per gram body weight.

Examination of these data reveals several significant facts. Storage of DDT in the body fat increases with level of administration. The fat accumulation is also profoundly influenced by the physical state of the DDT given. The toxicity observed in dogs with these dosages is similarly affected. No dogs, for example, have died from the 80 mg/kg/day dose of the dry solid DDT out of four, whereas the two dogs, 1–59 and 1–61, are the only ones of 16 that survived the 80 mg/kg/day dose of DDT dissolved in corn oil. One of these, we believe, would have also died had the dosage not been discontinued.

The fact that DDT disappears from the fat upon discontinuation of administration is demonstrated by examination of the data obtained in the case of the last two dogs in the table. Supporting evidence for appreciable fat storage in these animals at the time the treatment was withdrawn is the observed continuation of excretion of DDT metabolites in the urine of number 1–59 for 24 days and of number 1–61 for 16 days.

The distribution of DDT between subcutaneous fat and intraperitoneal fat was found to be equal in dog No. 1–35. This observation would indicate that the material is distributed uniformly throughout the fat depots in the body.

APPEARANCE OF DDT IN THE MILK

A third dog, 1–36, belonging to the group receiving 80 mg/kg/day solid DDT, had just weaned a litter during the course of this experiment. A small sample of milk was obtained upon each of two successive days and analyzed. DDT was found in amounts of 0.06 and 0.04 milligram per gram of milk, respectively.

A control dog, D–3, also with a litter was given a single 50 mg/kg dose of the ortho-para isomer of DDT, 2-o-chlorophenyl, 2-p-chlorophenyl-1,1,1-trichloroethane. Twenty hours later a sample of milk was obtained and found to contain approximately 0.05 milligram of the o,p-isomer per gram.

CONCLUSIONS

DDT in quantities of significance in its toxicological evaluation is stored in the body fat of dogs given daily oral doses. The storage increases with dosage level. Feeding oil solutions of DDT gives greater accumulation in the fat than does feeding the undissolved material. The accumulated DDT gradually disappears from the fat after discontinuation of administration.

The milk of lactating dogs receiving DDT or its ortho-para isomer contains appreciable levels of the respective compounds.

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SCIENTIFIC APPARATUS AND LABORATORY METHODS

A NEW TEST FOR BLOOD ESTROGEN

IT is well known that the vagina of the rat remains closed until sexual maturity but opens earlier in response to the administration of estrogens. The test here reported depends upon this phenomenon, but administration is made locally and in the 21-day rat is by this method positive to extremely small dosage.

The procedure is extremely simple. The sample, in

volume of 0.01 or 0.02 cc, is injected subcutaneously near the region of the future vaginal orifice and observations are made once daily. The first indication of a positive reaction consists of a crescent-shaped transverse dimpling of the skin at the developing vaginal orifice. Openings appear at various points in the crescent and fluid oozes at such slits from gentle pressure.

On the average it requires 4 or 5 days for the vaginae of two out of three animals to open; but easily recognizable changes appear usually within 24 hours. If large doses are used, for example, 0.005 mgm of estradiol diproprionate[1] in 0.02 cc of oil, the vagina may open within 24 hours and definite changes, easily recognizable at a glance, have been noted within 17 hours.

One of the chief objects in developing a delicate test for estrogen seemed to us to lie in its possible applicability to assays of estrogen in blood. To our amazement, if our calculations are even approximately correct, we found the test to be almost unbelievably sensitive to blood estrogens, for as little as 0.02 cc of untreated finger blood from women was always positive, while that from four different men was always negative.

For most of the experiments to date 21-day-old female rats have been used; but in one experiment six females of one litter of 16-day-old rats were used with such success that it seems possible that the 16-day-old rat may become the animal of choice for these experiments. The young were injected and returned to their mother. Within four days all the injected females had open vaginae: the two which had received 0.0005 mgm of estradiol in 0.02 cc of oil and the three that had received 0.02 cc of midcycle female blood. Within 30 hours the dimpling was observable. The one control showed no change.

How delicate this test really is, in terms of blood estrogen, is seen in the following calculation. Taking the recent figures of Markee and Berg[2] as a basis we find the midcycle titre of estrogen in the blood to be roughly 0.005 mgm per liter or 0.000005 mgm per cc. A positive reaction, involving anatomical changes, is thus attained with five one hundred millionth of a milligram of estrogen—which, however, still contains some billions of molecules.

The test, it is to be noted, costs nothing, for the test animals are not sacrificed, remaining perfectly normal members of a colony. Furthermore, the time required to make and read the test is almost negligible.

CARL G. HARTMAN
J. LITTRELL

THE UNIVERSITY OF ILLINOIS

[1] Generously furnished by Dr. E. Oppenheimer, research director, Ciba Pharmaceutical Products, Inc.

[2] J. E. Markee and B. Berg, *Stanford Med. Bull.*, 2: 55, 1944.

NORELAC—A SUBSTITUTE FOR SHELLAC IN THE PRESERVATION OF SMOKED PAPER RECORDS

NORELAC (*No*rthern *Re*gional *Lac*quer) is a new thermoplastic polymer developed at the Northern Regional Research Laboratory.[1] The properties of Norelac[2] and its solubility characteristics encouraged us to test its use as a substitute for shellac in the preservation of smoked-paper records, such as the kymograph records produced in physiological and pharmacological laboratories. The present war-time shortage of shellac has emphasized the need for a good substitute. Even when shellac is plentiful the preparation of a suitable coating for smoked records is something of a nuisance, and can not be done in a short time. A rather voluminous alcohol-insoluble residue must be allowed to settle and the supernatant solution decanted.

A few experimental trials with Norelac in a suitable solvent demonstrated readily that it can be substituted for shellac with complete satisfaction. A 5 per cent. solution of Norelac in a mixture of isopropyl alcohol and Skelly Solvent "C" (or naphtha) makes a good protective coating for a smoked-paper record. The record dries in ten minutes with a dull finish. If less than 5 per cent. of Norelac is used, abrasion marks are easily produced. If 10 per cent. of Norelac in isopropyl alcohol and Skelly Solvent "C" is used, the record dries free from tack in ten minutes with a glossy finish. The record can be given an intermediate degree of luster by the use of 7.5 per cent. of Norelac in a mixture of 75 to 85 parts of isopropyl alcohol and 25 to 15 parts of Skelly Solvent "C." The coating is applied to the smoked paper in the manner usually employed with alcohol solutions of shellac. The records coated with Norelac lie flat without curling, and can be stored flat or rolled without danger of sticking, marring or cracking. The addition of 1 to 2 per cent. of paraffin[3] will reduce any tendency to stick under unfavorable conditions of storage.

The sample of Norelac used had an iodine number of 89.2, indicating that there would be no danger of spontaneous combustion of stored records. A solution of Norelac has also been found suitable for protection of paper labels on reagent bottles and laboratory equipment.

It is convenient to prepare a stock 30 per cent. solution of Norelac in 99 per cent. isopropyl alcohol with the aid of heat, and to dilute as required for use to 5 or 10 per cent. or some intermediate concentration with a mixture of isopropyl alcohol and Skelly

[1] J. C. Cowan, A. J. Lewis and L. B. Falkenburg, *Oil and Soap*, 21: 101–107, 1944.

[2] Obtainable from General Mills, Inc., Minneapolis, Minn.

[3] J. C. Cowan, L. B. Falkenburg and A. W. Schwab, *Modern Packaging*, 17: 113–119, 1944.

Solvent "C." If the solution prepared for use contains more than 25 per cent. of Skelly Solvent "C" it tends to cause creeping of the carbon on the paper; and if the concentration of Skelly Solvent "C" is less than 15 per cent., the solution tends to cloud or deposit an amorphous precipitate. Solutions of 5 to 10 per cent. of Norelac and up to 25 per cent. of Skelly Solvent "C" tend to jell when stored at 5° C., but remain fluid at 20° C.

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DISCUSSION

BREAD "ENRICHMENT"

THE appearance of an article under the above title by Dr. E. V. McCollum[1] calls for a reply in view of Dr. McCollum's long-established eminence in the field of nutrition. We do not differ from Dr. McCollum in nutritional principles. We do differ strongly with him on the practical efficacy of his proposed approach to the problem of our bread (and flour) supply. The practical problems, as well as the nutritional aspects related to them, have been the subject of extended discussions in the Food and Nutritional Board ever since its oganization in November, 1940. Dr. McCollum has been present at many of these discussions, often as a silent listener, but this is the first time he has come out publicly in opposition to the judgment of the majority of the board.

Dr. McCollum's position on bread "enrichment" is unrealistic in respect to feasibility of achievement. He treats of bread with little recognition of the fact that there are several million Americans who do not regularly use bakery bread but homemade bread. There is a notably high incidence of deficiency disease in the "hot bread belt" of our South. This fact his article ignores. No adequate national program can be based on a consideration of bakers' bread only.

Dr. McCollum "would prefer to see bread improvement achieved by a legal requirement concerning the minimum skim milk solids to be included in bread." He does not say how he would apply it to homemade bread. This is a serious omission in view of the fact that the "hot bread belt" is also an area of low milk supply. The Food and Nutrition Board always has and continues to favor strongly the continuation and extension of the use of milk solids in baker's bread, a practise which was already widely in use before enrichment was inaugurated and which we confidently believe will continue in the future. Addition of milk to bread, however, does not significantly liberalize the supply of thiamine and niacin in the dietaries of low income groups, especially not in the South.

He says "'The bread program of Canada and England seems to me to be superior to our own." That of England is a war program born of the threat of a food blockade. It sought to stretch the supply of wheat which it might be possible to import and to use home-grown foods as far as possible. A reflection of this is the fact that Britain has prohibited the sale of any bread within 24 hours after it comes from the oven. To so limit the available supply of bread to a somewhat stale quality facilitated the nationally necessary substitution of potatoes for bread. No such condition applied in the United States and it is reasonable to suppose that it will not continue to apply in England. Will England's "long extraction" program survive in peacetime? Switzerland's very similar program of 1936–1937 failed within a year.

Canada's program was undertaken nearly simultaneously with our own and like our own was on a voluntary basis. Conditions of wheat supply also were similar to our own. Extent of success is measured by the comparative volumes of bread and flour affected, namely, about 7 per cent. of Canada's consumption versus 70 per cent. or more which had been affected by enrichment in the United States before January, 1943.[2] Dr. McCollum at a later point in his article admits by clear implication the present infeasibility of the Canadian program. He says "If the milling industry were decentralized and mills were located in the vicinity of all centers of population . . . the manufacture of . . . Canada Approved Flour . . . would be practicable." Does he feel that an impracticable program is "superior to our own"?

Dr. McCollum recommends the use of wheat germs, corn germs, yeast and soyflour as bread improvers. Their use has been advocated before and the products have their merits, but in no sense are they presently available as popularly acceptable substitutes for enrichment nor in significant quantities of adequately controlled quality. To advocate their use in lieu of enrichment would postpone indefinitely any effective action. Any systematic program of bread and flour improvement based on the use of these ingredients would be even more difficult to introduce than a general substitution of whole wheat flour for white flour. Either expedient is for reasons of custom and present business organization a generation or more away as a general remedy.

Dr. McCollum objects that "the name 'enriched' connotes a higher quality than the enriching ingredients confer upon white flour. . . . The term 'improved'

[1] *Bulletin of the Maryland State Health Department*, 17, No. 1, March, 1945.

[2] In January, 1943, War Food Order Number One made enrichment of all white pan bakers' bread mandatory for the duration of the war.

would more nearly express the facts." We trust, however, that Dr. McCollum will not base his opposition on the choice of a word. The word "enriched" was not the present writer's original preference and indeed it was received at first with disfavor by many of the early proponents of the program for flour and bread improvement. However, in public affairs one must make his choice on the basis of overall considerations, not upon some minor departure from his preference. That is essential to the democratic process.

The word "enriched" was the choice of the Federal Security Agency which is charged by law with the enforcement of the Food, Drug and Cosmetic Act. Under accepted terminology of the trade, "flour" is synonymous with "white flour" and the improvement of white flour by addition of the important specified ingredients was judged sufficient to justify the term "enriched." The term is now so well known that it has acquired a meaning which is well understood.

One may fully subscribe to Dr. McCollum's nutritional ideals and yet without disrespect to his scientific opinion decide to support an instrument for an "improved" flour and bread which has been forged in the hot fires of prolonged and often tedious public hearings, which has been submitted to the test of trial in the Supreme Court and has commanded the support of the industries concerned, as well as that of a large body of able and disinterested nutritionists. Although it might formulate proposals which would better conform to its scientific opinions, no purely scientific body, working alone, could hope to forge an instrument as effective as this has been in enlisting the cooperation of scientists, industrialists, government administrators and the consuming public. None of these factors of society can be neglected in framing a public health measure. Effective action must be taken in the light of custom and existing legal precedent as well as in the light of scientific principles. It is the social, industrial and legal background which Dr. McCollum has failed to appreciate in offering his criticisms.

ROBERT R. WILLIAMS

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DR. WILLIAMS'S statement that my article in the *Bulletin of the Maryland State Health Department* was the first public expression of disapproval of the bread enrichment program requires correction. I was not a member of the Food and Nutrition Board until after the bread enrichment program had been adopted as a policy of the board. When, about February first, 1941, I was requested to lend my signature to a press release announcing the approval of the program by most of the members of the board, I declined to do so. At that time I made my position concerning the enrichment proposal clear. On November 3, 1944, I participated in a conference in Detroit under the sponsorship of the Research Laboratory of the Children's Fund of Michigan. My paper was published in the Proceedings of the Conference.[1] I voiced much the same criticism of the bread enrichment program as was contained in the paper Dr. Williams referred to. I feel certain that every member of the board has long known of my objections to it.

In the manufacture of refined wheat flour a score or more of essential nutrients present in significant amounts in the wheat kernel are removed. To give such flour, supplemented with three vitamins and iron, so good a name as "enriched" is misleading. It overstates the value of the flour in the mind of the consumer who lacks technical knowledge concerning foods. The proposed legislation requires the addition of three vitamins and iron, but does not require the inclusion of such ingredients as skim milk powder, wheat or corn germs, or dried yeast, all of which could be used, and if included in suitable amounts would make bread nutritionally superior to that containing only the required enriching ingredients.

In normal times there is a great abundance of skim milk for the manufacture of milk powder for baker's use. I am informed that there is presently filtered out of beer annually the equivalent of about thirty million pounds of dry yeast. Only about three million pounds of dry brewer's yeast was prepared because there was no market for the rest, which was discarded as waste. At the request of governmental agencies the brewing companies dried about twenty million pounds of beer yeast in 1944, but representatives of the brewing industry have assured me that they have no expectation that they will have a market for much of the yeast they make after the war is over. The distilling industries make much more yeast than do brewers, and most of this is wasted, not even being used for animal feed. There is now manufactured about one hundred million pounds of wheat germs having not more than 10 per cent. of non-germ substances; and about four hundred million pounds of corn germs. Doubtless more of each of these germs would be manufactured if there were an outlet for them. These suggested additions to the bread mix are precious sources of nutrients. It seems folly for us to enforce by law an ineffectual supplementing of white flour when a much more sound policy for improving bread seems entirely practicable if promoted with effective leadership.

The writer has examined loaves made with 6 per cent. of skim milk powder and in addition dried yeast, wheat and corn germs in amounts up to 3 per cent. of the dry matter of the bread mix. Eleven combinations of the three last-named ingredients were

[1] "Implications of Nutrition and Public Health in the Postwar Period." Detroit, Michigan, 1944.

used. There was small reduction in loaf volume and the loaves were darker in color as compared with the loaves without the yeast or germs. The texture was not such as would be rated highest by any expert scorer, but all were attractive and had excellent flavors. It should be pointed out that every criterion of quality upon which commercial breads are judged, such as loaf volume, oven break, external and internal color, crumb, etc., represent fictitious standards having no relation whatever to nutritive value of the bread.

Bread is a low-cost food. It is a basic staple. Nothing more effective in safeguarding the nutritional status of the poor can be done then to encourage the making and consumption of bread of the highest possible nutritive value. It should be so nutritious that it can make good most of the deficiencies of any other foods included in a simple and monotonous diet. The inclusion of the ingredients recommended would go a long way toward accomplishing this objective. This can not be said of the presently promoted "enriched" bread.

Dr. Williams is correct in stating that I have ignored sociological, industrial and legal precedent in my recommendations concerning bread improvement. It has long been my belief that eventually industry must adjust itself in matters involving foods to the physiological needs of consumers. For this reason I have offered suggestions concerning what bread should be composed of with no other objective than to acquaint the public with facts which are supported by scientific investigations. Success in putting into effect such a bread program would seem to be no difficult undertaking, provided the plan has the support of scientific and industrial leaders whose primary interest is safeguarding the nutrition of the people.

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ONE-PARENT PROGENY OF TUBIFICID WORMS

In a five-years' study of the activities of tubificid worms (*Tubifex* and *Limnodrilus*) it is indicated that these hermaphroditic forms are apparently able to effect self-fertilization and to produce young. Supporting this statement are the results from nine one-worm cultures, each treated as follows:

(1) The worm was isolated shortly after birth when about one week old. (2) Was placed in a shell vial with 0.5 cc or less of mud examined under x20 (approximately) to make sure that no additional worms or their eggs were present. (3) Was fed weekly by adding autoclaved sewage solids, in suspension. (4) When young worms appeared, they were removed from the culture.

The worms become sexually mature in three or four months after birth. Six of the above one-worm cultures, now about seven months old, have to date (late March, 1945) produced 208 young. Another worm isolated as above and now more than two years old produced 19 young during its first year and 148 during its second year.

My first observation of the above phenomenon occurred on August 11, 1943.

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SCIENTIFIC BOOKS

RELATIVITY

The Meaning of Relativity. By Albert Einstein. 135 pp. Princeton, N. J.: Princeton University Press. 1945. $2.00.

The book is a reissue of a book first presented in lecture form at Princeton University in 1921, and published by Methuen and Company in Great Britain and by the Princeton University Press in the United States. In this edition an appendix extending the theory of relativity to the "Cosmologic Problem" is added. Attention is also called to other developments, among them the solution of the fundamental problem—so long delayed—in which the law of the "geodesic," which, in the classical treatment, is superposed upon the law of the field equations, is shown to be the analytical equivalent of the restriction placed upon the motions of the singularities by the fact that the equations are non-linear.

The main text is divided into four chapters—"Space and Time in Pre-Relativity Physics"—"The Theory of Special Relativity"—"The General Theory of Relativity"—"The General Theory of Relativity (Continued)."

The treatment follows what may be called normal lines and, coming from the "Father of Relativity," is naturally authoritative and interesting in approach. It is, moreover, concise and to the point.

As to how far the book fulfils the promise of its title is to some extent an open question. It is often characteristic of one outstanding in originality that the concepts which are real and which form the workable elements of his thinking are, to a considerable extent, individualistic. They are apt to be strong and occupy positions of very positive conviction. Indeed, is it not the strength of these convictions which provide the stimulus for discovery? Sometimes, how-

ver, the result is something which does not so readily ppeal to the thoughtful reader; for in order to be tune with the author he has to supplement the old logic of mathematical formalism with a kind f faith in the meaningfulness of the concepts. It is ecessary to adopt a reasonably sophisticated approach to understand the theory of relativity at all. et if one becomes too sophisticated, he is apt to ecome troubled by such things as clocks and scales s bases for the arguments and wonder how far he n postulate things about these mechanisms. He onders in what sense the author is thinking of such concept as an electric field, for example. Also, ings often fail to get defined carefully in the elentary books because it is supposed that such phistication is for the advanced books, and they ever get defined in the advanced books because these ooks seem to be no place for such elementary matrs of definition. So one arrives at a kind of comunity of procedure in which all "in the know" do e same thing, even though it is not always clear as what is being done.

Of course, one may write his own charter of underanding, and say that scales and clocks are simply mbolic ways of recognizing that we have certain rocedures for assigning numbers x, y, z and t to the ents, these procedures involving in part measureents and in part calculations which are supposed correct the measurements for light velocity and so rth, and that the result of all this is symbolized by e statement that the scales and clocks give such and ch numbers for the events. If, however, the reader comes too sophisticated in this matter, he will find at he will depart from the spirit of the author's tent, either because of the unexpressed meaning hich it is intended to attach to the concepts, or beuse the author has purposely tried to avoid what ppear to be complexities of exposition. If the ader persists in his heresies, he will become worried the meanings to be attached to the behavior of ocks and scales when set in motion relatively to one nother—even the Michelson and Morley experiment ill lose some of its dignity, and he will become conious of the need of certain other principles to preve for his scales and clocks a respectable existence the realms of logic.[1]

Then, in the matter of the general theory, many stuents of relativity may have squirmed at the apparent portance of "light" in the matter. Indeed, it is ossible to regard the famous constant "c" as appearg in another way—a way more in harmony with the tronomical surroundings.[2] If one does this, however, he will find that many relativists will regard the procedure as almost of the nature of desecrating something very "holy."

A rather long discourse of this kind would be quite out of place in a review, particularly of a book by an author so eminent, were it not that the *meaning* of the word "Meaning" is involved. The purpose of this review is not so much to present a criticism in this matter as to emphasize the fact that, in seeking a *meaning* of an author's presentation, more is necessary than an understanding of the mathematics—more is necessary than an ability to reformulate the subject to one's own satisfaction. It is necessary to obtain as clear a picture as possible of the mental attitude of the author and of his various concepts, so that he may immediately know what is meant by such a statement as "From all of these considerations, space and time data have a physical real, and not a mere fictitious, significance" (page 29). Alas, to obtain such a picture is not easy. To each one of us the pictures in the mind are things of his own, and the values which he places on the various elements are things of his own making.

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[1] Some of these matters are discussed in a paper by . F. G. Swann, *Rev. Mod. Phys.*, 13: 197, 1941.

[2] See, for example, W. F. G. Swann, SCIENCE, 62: 145, 925. Also *Rev. Mod. Phys.*, 2: 243, 1930.

WOOD CHEMISTRY

Wood Chemistry. Edited by LOUIS E. WISE, of The Institute of Paper Chemistry, Appleton, Wisconsin. A.C.S. Monograph Series No. 97. 900 pp. New York, N. Y.: Reinhold Publishing Corporation. June, 1944. $11.50.

THE general field of wood chemistry has expanded greatly in the last few years as wood has been called upon to fill an increasing role in the needs of our nation. The book, "Wood Chemistry," seeks to bring together the views of some of America's best-known specialists in the field. The book contains 25 chapters and seeks to give as complete a picture as possible of the properties and possibilities of wood as a chemical material.

Part I, "The Growth, Anatomy and Physical Properties of Wood," gives the reader a conception of wood as a complex material of plant origin. The functions of the various parts of the tree, how the tree grows and the differences between hardwoods and softwoods are described. A chapter on the physical properties of wood gives those properties that are of importance in the use of wood as an engineering material.

Part II, "Components and Chemistry of the Cell Wall," deals with the principal components of the cell

wall—cellulose, hemicellulose and lignin—giving their chemical constitution, relative relationships in the cell wall, chemical reactions, changes that occur when subjected to various chemical reactions, physical-chemical properties and the production and properties of derivatives. Comparisons are made frequently to cellulose from cotton to bring out differences and similarities. Information on x-ray studies and methods of molecular weight determination is given for both cellulose and its derivatives. Methods of isolation and study for both hemicellulose and lignin are described. Research on these two wood components has not progressed to the state of that for cellulose, and the authors of the two chapters illustrate that fact by giving the various points of view.

Part III, "The Extraneous Substances," points out the various types of materials that occur in wood as volatile oils, resins, fats, fatty acids, sterols, waxes, dyes, pigments, tannins, free carbohydrates, saponin and other extractives. The author has developed the field very well and, in addition, presents a procedure developed by himself for the isolation of these various extraneous substances.

Part IV, "Surface Properties of Cellulosic Materials," reviews such properties as adsorption by gases, water vapor and liquids, hysteresis, fiber-saturation point, selective adsorption, swelling, shrinking, antishrink treatments, electrical properties, diffusion, drying and solvent seasoning.

Part V, "The Chemical Analysis of Wood," describes various methods employed in analysis of wood and wood components and their significance in the chemistry of wood.

Part VI, "Wood As an Industrial Raw Material," describes the use of wood for fuel, for the production of chemical products through wood distillation, for the production of pulp and paper by chemical pulping, for sugar production by hydrolysis, for the production of oxalic acid by caustic fusion, for liquid products by hydrogenation and for wood plastics after chemical pretreatment.

Chapters 24 and 25 describe the decomposition of wood and wood products as brought about by various organisms and fungi.

Each chapter is supplied with a large list of references that show the scope of the work covered in the book and the thoroughness of the authors in the development of their chapters.

ELWIN E. HARRIS

THE ANALYSIS OF FOODS

The Analysis of Foods. By ANDREW L. WINTON and KATE BARBER WINTON. 999 pp. New York: John Wiley & Sons. 1945. $12.00.

THOSE familiar with the four volumes of "The Structure and Composition of Foods" by the same authors will not be disappointed in the present work, which is a compact but complete handbook on methods employed in food chemistry. The scope of the book is as vast as our knowledge of those aspects of organic and biological chemistry which have any bearing on food analyses. It towers without equal in the field for precision, clarity and breadth of subject-matter. There is hardly a method which is omitted, hardly a reference overlooked. It is a vast and laborious task, but one which will be amply rewarded by the gratitude of all workers who will have recourse to it.

A brief introductory section, describing such basic apparatus as refractometers, colorimeters and photometers, and citing the common reagents employed, is followed by a division of the bulk of the book into two parts. Part I deals with general methods for the analyses of organic elements, constituent groups such as water, protein, fat, nitrogen-free compounds, fiber and ash, as well as alcohol, vitamins, natural and artificial colors and preservatives. Part 2 describes methods adapted to special foods such as cereals, fatty foods, vegetables, fruit, saccharine foods, beverages, dairy products, animal foods, alkaloids, flavors, spices and yeast. There is an abundance of helpful diagrams, photographs and tables and an excellent index. Several descriptions have been put to the test by students who had had no previous knowledge of the methods described. Invariably the results proved that the instructive messages of the texts were fully comprehended and readily followed and that the desired results were obtained. "The Analysis of Foods" is an indispensable tool to all laboratory workers in the field.

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